

***Biotron*** *ASX:BIT*

**AGM 8 November 2013**

***Biotron***



# Milestones 2012/13: Planned vs Achieved

ACTIVITY	STATUS	OUTCOME
Complete Ph 2a HIV trial (1Q2013)	✓	Positive data reported
Complete Ph 2 HIV/HCV co-infected trial (1H2013)	✓	Positive data reported
Conduct bioequivalence study in healthy volunteers with new BIT225 capsule formulation (1H2013)	✓	Positive data reported
Complete the three-month toxicology studies (1H2013)	✓	Supports three-month trial
Commence three-month Phase 2b HCV trial (2H2013)	✓	Trial initiation site visit scheduled
Progress BIT314 through process development, scale-up activities, and preclinical toxicology studies		On hold to conserve funds and focus on BIT225
Report follow-up data from Ph 2a HCV trial	✓	Positive 48-week follow-up data reported

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# GLOBAL PERSPECTIVES

**Progress in development of new HCV drugs has been rapid over last 12 months**

- **Update of field**
- **What does that mean for Biotron's HCV program?**
- **Update on BIT225 Programs**
- **Outlook**



# HCV - Background

- 180 m people infected worldwide (3% world population); 130 m are chronically infected
  - HCV is 4x more prevalent than HIV
- 4 m patients in US (2.7 m chronically infected)
  - 75% are undiagnosed
  - Baby boomers - >800,000 cases undiagnosed (CDC)
    - 5x more likely than other adults to have HCV
- Majority of infected patients remain untreated or untreatable
  - Standard of care, until very recently, has been interferon and ribavirin
    - Associated with side effects and ineffective in ~50% of patients
  - Significant side effect profile – high drop out rate
- Documented need for new, safer, direct-acting antiviral (DAA) drugs

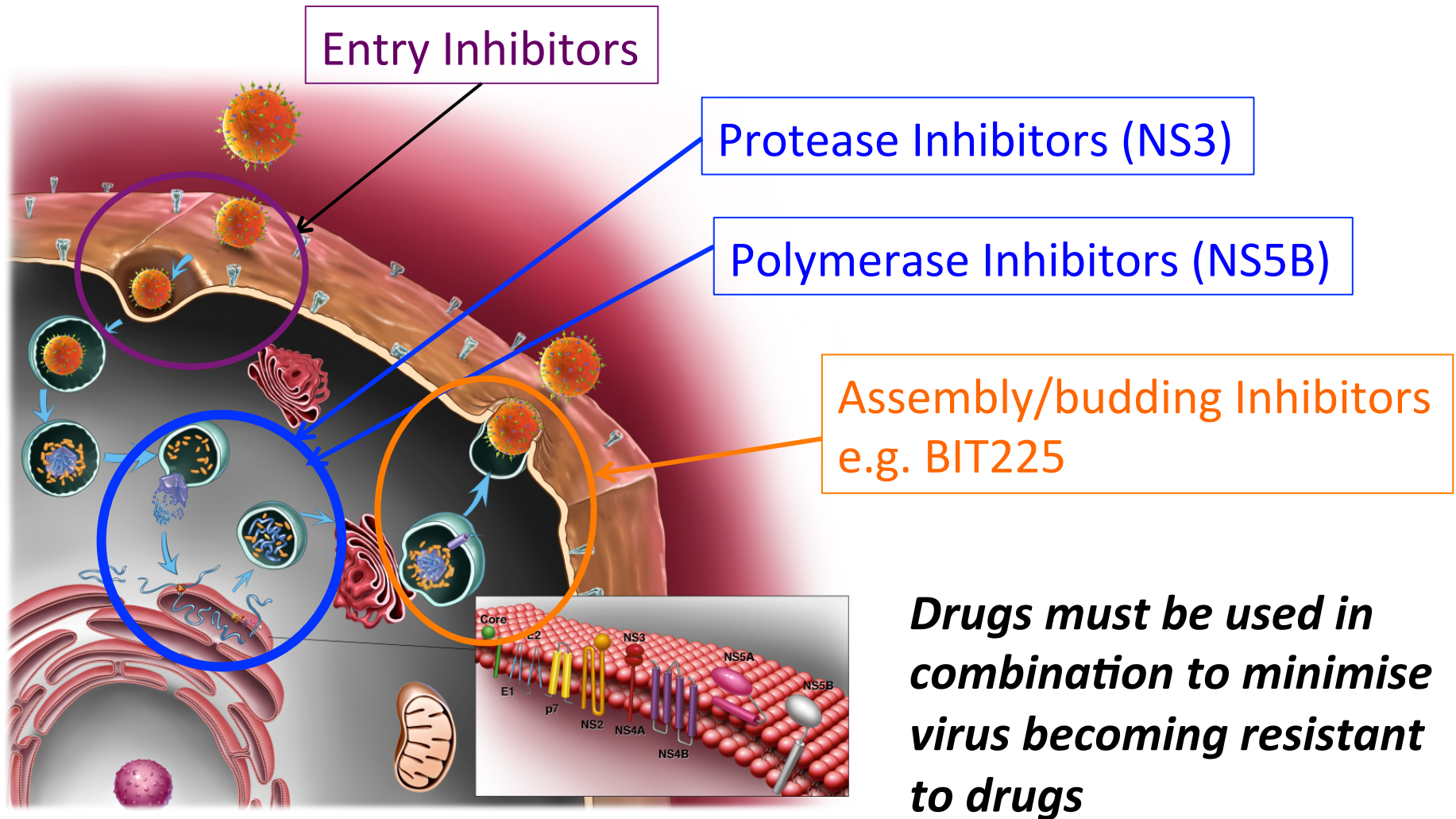


# Current Treatment Options

- Standard of care treatment has been interferon and ribavirin (IFN/RBV)
  - 48 weeks of treatment
  - Associated with debilitating side effects in many patients
    - High drop out rate
  - Ineffective in ~50% of cases
    - Genotype 1 particularly resistant to IFN/RBV
- Industry focus has been on developing new drugs that directly target the virus i.e. **Direct-Acting Antivirals (DAAs)**
- Wish list:
  - All oral drug regimens
  - Less toxic drugs
  - Pan-genotype drugs that target all HCV genotypes 1 – 6
  - Shorter treatment periods
  - Effective treatment options for hard-to-treat populations  
e.g. HIV/HCV coinfecting population



# Selected Classes of HCV DAA's



***Drugs must be used in combination to minimise virus becoming resistant to drugs***

# Current HCV DAA Approval Landscape

## **Protease Inhibitors**

- First generation approved in 2011/12
  - Boceprevir and Telaprevir
- Second generation expected to be approved late 2013
  - Simeprevir (SIM; Janssen)
    - Expected to replace Boceprevir and Telaprevir

## **Polymerase Inhibitors**

- First approval expected in late 2013
  - Sofosbuvir (SOF; Gilead)

## **2014 and beyond**

- Expect additional filings for approvals
- New DAAs and new combinations of DAAs





# Current DAA Treatment Outcomes – Gen 1 and 2 Selected Overview

## **Genotype 1**

- Most common variant in USA, Europe and Australia
- New DAAs (with and without IFN+/- RBV); 12 weeks therapy
  - Overall cure rates (SVR12)
    - Non-cirrhosis ~92%
    - Cirrhosis ~80%

## **Genotypes 2, 4, 5, 6**

- Respond well to 12 weeks of SOF + RBV (and others)
- Low relapse rate

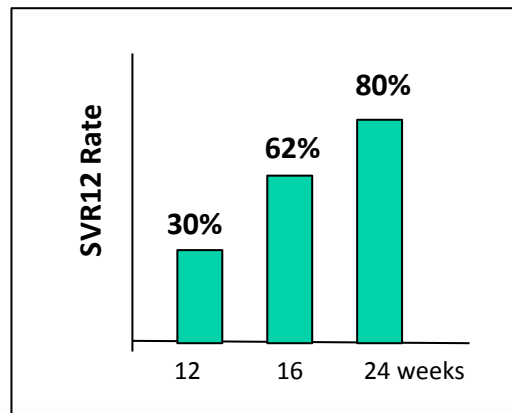




# Selected Current DAA Treatment Outcomes – Genotype 3

## Genotype 3

- Higher prevalence in lower socio-economic groups
- Predominant variant in Asia
- Large proportion of future cases expected to be gen 3 (intravenous drug users)
- Treatment with new DAA classes is more problematic than Gen 1 and 2
  - SOF + RBV requires at least 24 weeks dosing  
OR
  - Need to add IFN back in i.e. SOF + RBV + IFN



# Why Additional Classes of DAAs Are Still Needed (For All Genotypes)

- SOF, SIM etc have only been assessed under trial conditions
  - Treatment decisions are being made on limited trial data (often Ph 2)
- Real world will impact on SVR rates post-approval
- Patient compliance with taking drugs for extended periods
- Additional drugs may reduce treatment times (ideally to 4 weeks) and COST
- Potential for resistance unless multiple classes of drugs (as per HIV)
- Specific groups not well served with latest drugs, e.g.
  - Cirrhotics
  - Gen 3

**No longer one single standard of care – multiple treatment strategies on basis of genotype, disease stage, etc**



# HIV/HCV Co-Infected Population

- One third of HIV-positives are infected with HCV
- Rapid progression to liver failure
- Respond poorly to IFN/RBV
  - ~ 19% SVR rate
- Often an after-thought in trials of new DAAs
- Drug-drug interactions limits use of protease inhibitors (i.e. Boceprevir, Telaprevir and Simeprevir) in these patients
- Limited classes of new DAAs to combine with SOF in this population
- Recent data from SOF + RBV:
  - Genotype 1            76% SVR
  - Genotype 2            68% SVR
  - Genotype 3            67% SVR



# BIT225 and HCV

- ✓ Novel, oral, small molecule compound
- ✓ Only one of its class (p7 inhibitor) in clinical trials
- ✓ Inhibits viral assembly; active at later stage of virus life cycle to polymerase and protease inhibitors
- ✓ Clinically active against HCV genotype 1 (1a and 1b) and genotype 3
- ✓ Doesn't readily generate resistance
- ✓ Also active against HIV

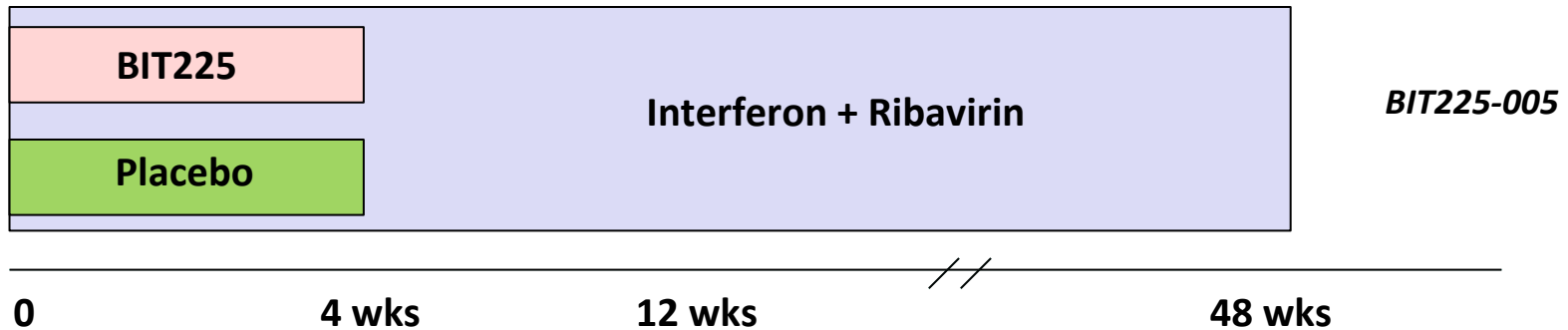
**“Hepatitis C market is forecast to grow by 230% peaking at \$15.5bn in 2022”**

*Source: Datamonitor Healthcare*

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# BIT225 – Proven Clinical Activity Against HCV



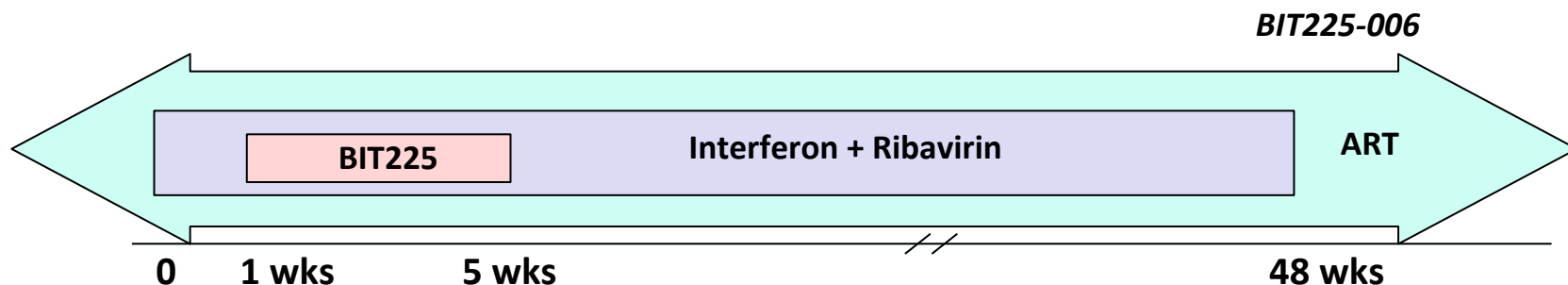
Treatment	12 WEEKS Early Virological Response*	48 WEEKS Sustained Virological Response*
400 mg BIT225 + IFN/RBV	86%	<b>100%</b>
200 mg BIT225 + IFN/RBV	88%	88%
Placebo + IFN/RBV	63%	75%

*\*virus levels below limit of detection i.e. 50 IU/ml*

**Clear demonstration that BIT225 has good antiviral activity in hard-to-treat, treatment-naïve HCV genotype 1 patients**

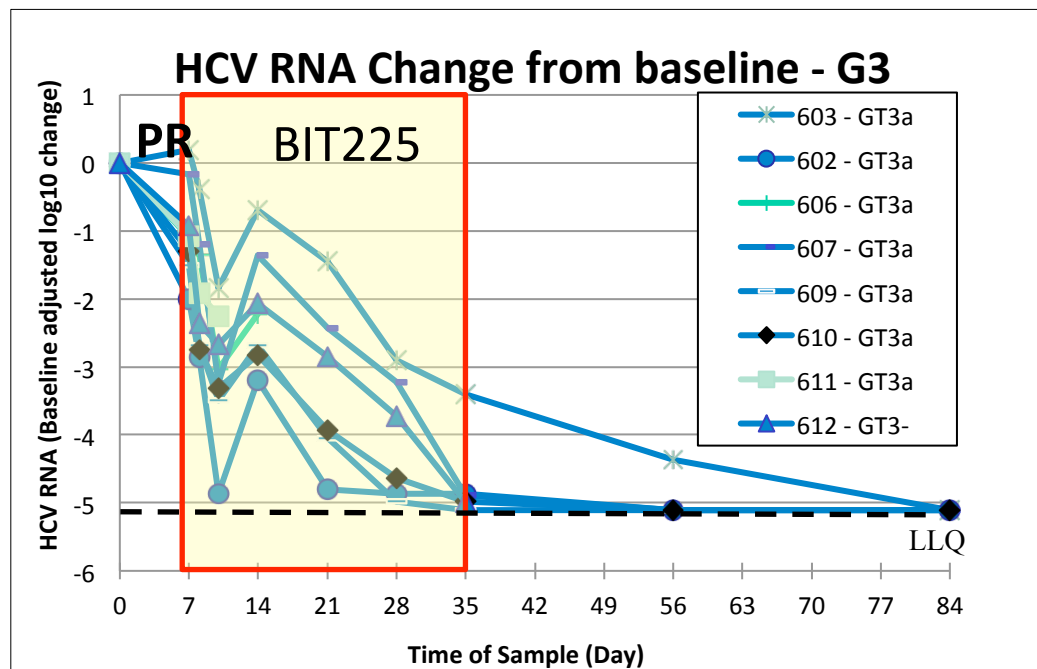
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# BIT225 – HIV / HCV Co-Infected Trial



- **Phase 2 HIV/HCV trial - completed clinical phase in July 2013**
  - Genotypes 1 and 3; 28 days dosing in combination with IFN/RBV
  - Treatment-naïve to HCV treatment with RBV and/or IFN; HIV controlled by antiretroviral drugs (ART)
  - *Interim 12-week data presented at AASLD conference in Washington DC this week*

# BIT225 – HIV / HCV Co-Infected Trial (cont)



- At 12 weeks - All HCV genotype 3 patients who completed treatment were clear of virus
- Rate of decline in virus levels increased after addition of BIT225 at day 7
- BIT225 enhanced effect of IFN/RBV in HIV/HCV co-infected patients



# BIT225 – HIV / HCV Co-Infected Trial (cont)

- Genotype 1 response was impacted by a genetic change in IL28B in two patients – this means that they are unable to respond to IFN/RBV
- Data from previous 005 trial demonstrated that BIT225 works in gen 1's
- This trial demonstrates that:
  - **BIT225 is active in gen 3**
  - **BIT225 improves outcome for hard-to-treat HIV/HCV co-infected patients**
- Data provides guidance for positioning BIT225 and design of future trials



# Why Are We Using IFN/RBV in BIT225 Trials?

- Drugs to treat chronic viral diseases such as HIV and HCV can't be used on their own
- IFN/RBV has been the only approved treatment for HCV
- Other new DAAs have also been trialled in combination with IFN/RBV
- IFN/RBV + DAA combination data is used to determine what genotypes/patient populations, etc that the DAAs work against
- IT DOESN'T MEAN THAT BIT225 IS BEING POSITIONED TO BE USED WITH IFN/RBV
- BIT225 can be trialled in combination with other DAAs once they are approved



# Where Do These Results Position BIT225 in the New DAA World?

- BIT225 works against HCV genotypes 1 and 3 Well positioned for genotype 3, which has greatest unmet need
  - All patients finishing treatment responded with just 28 days of BIT225
  - Potential to add to new DAAs e.g. SOF + RBV to improve outcomes with shorter treatment duration in this genotype
- HIV/HCV co-infecteds have particular unmet need
  - Potential to be a second DAA class to add to polymerase inhibitors as protease inhibitors are problematic for this group
    - Do not expect drug-drug interaction issues with BIT225 on basis of in vitro studies and outcome of the HIV/HCV co-infected trial

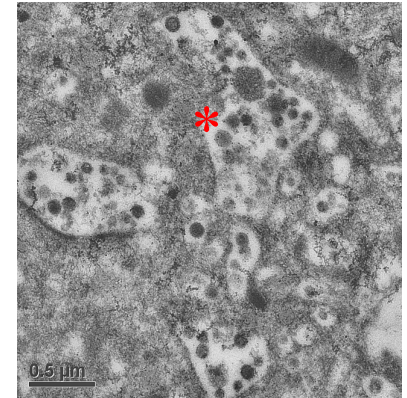
**BIT225 has added advantage due to its unique anti-HIV activity**



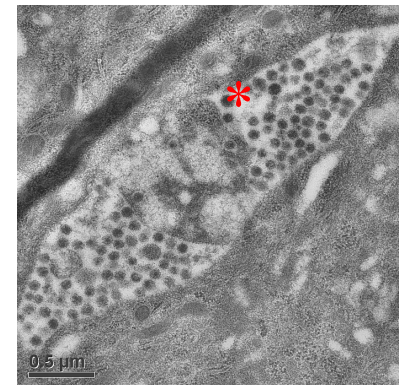
# HIV – Towards a Cure

- 34 million people worldwide living with HIV
- Anti-HIV drugs (ART) have improved the quality of life for HIV+ patients
- BUT – ART does not eradicate HIV infection
- Sustained, low-level HIV replication occurs in ART-treated patients
- Reservoirs of infection hide virus from the immune system and ART
- Industry is now focused on developing drugs to eradicate or cure HIV infection
- **BIT225 is active against HIV in the monocyte-derived macrophage reservoirs**

**Reservoirs are last of the holy grail in HIV treatment**



**+BIT225**



**Control**

# BIT225 – Proven Clinical Activity Against HIV

- Phase 1b/2a randomised, placebo controlled, double-blind trial (BIT225-004)
  - 24 patients, HIV-1 positive, treatment-naïve
  - 10 days dosing with BIT225 (monotherapy)
- **Results demonstrated that:**
  1. **BIT225 significantly reduces HIV levels in the macrophage (reservoir) cells in HIV-infected subjects**
  2. **BIT225 can cross the blood-brain barrier, opening up the possibility of treatment of AIDS-related dementia**

**Results support a potential role for BIT225 in cure/eradication strategies**

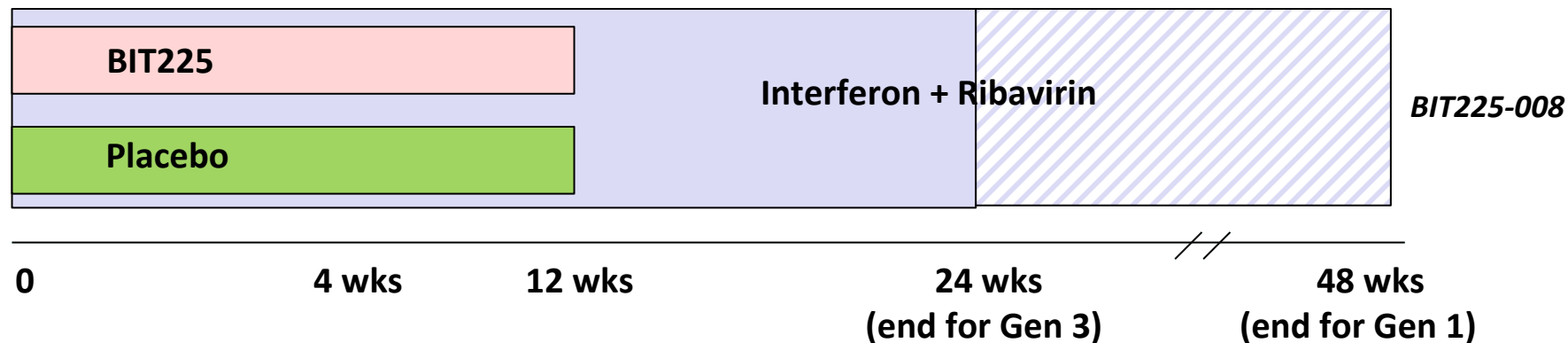


# BIT225 – Stepwise Progression to Commercialisation

- Strategy is guided by:
  - Advisory panels of US-based KOLs who are leaders of the field
  - Interaction and feedback from US healthcare analysts who specialise in antiviral space
  - Interaction and feedback from potential partners
- Biotron continues to engage with industry at different levels
  - One-on-one meetings
  - Presentations at US corporate healthcare events
  - Presentation of key data at major medical/scientific conferences, including prestigious late-breaking sessions
- Potential partners have been caught up in rush to market with other classes of DAAs
  - Now know the DAA treatment gaps
  - Now know at least 12 weeks dosing is required with current DAAs



# BIT225 - HCV Phase 2 Three-Month Dosing Trial



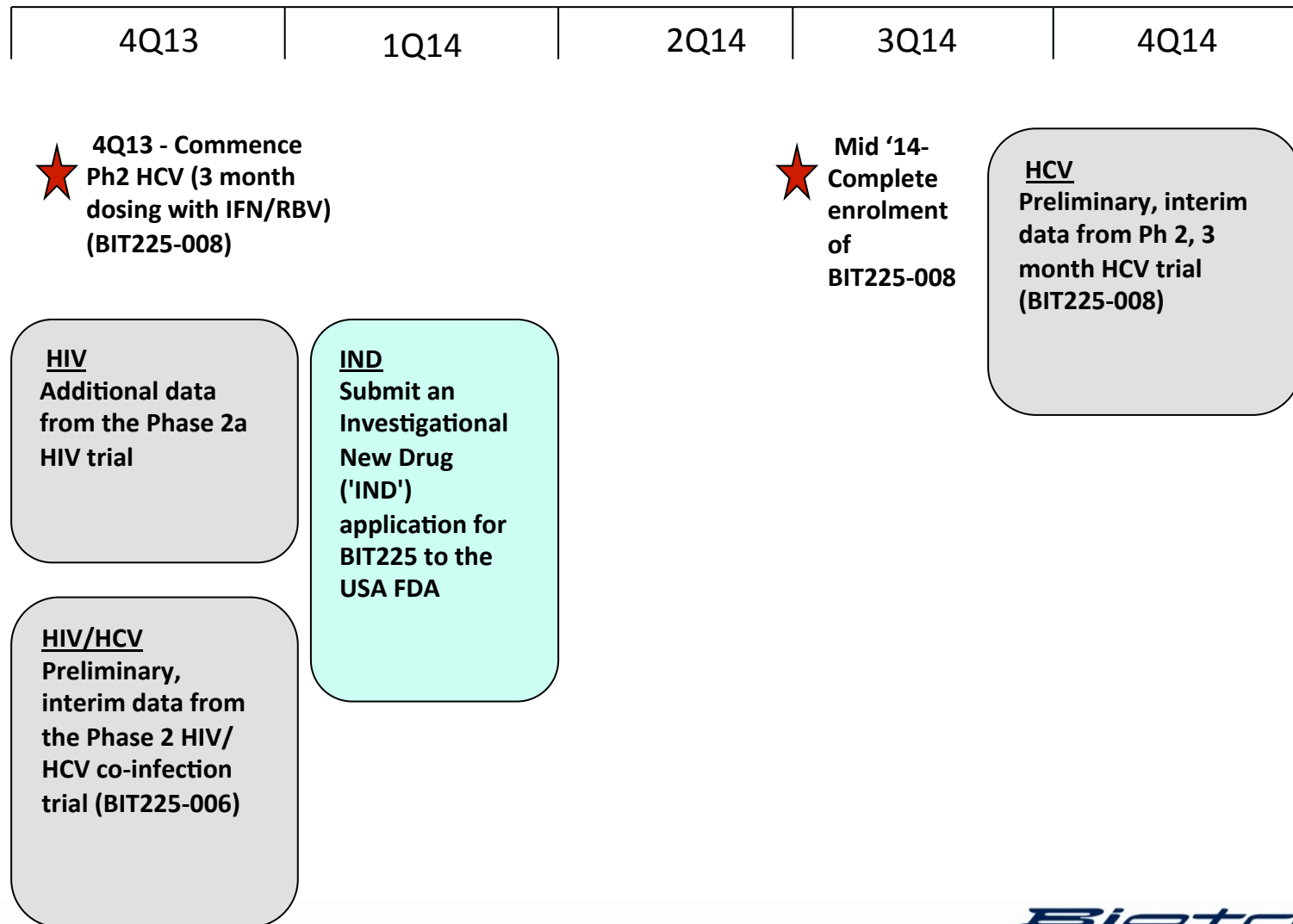
- Randomised, placebo-controlled, double-blind trial
- 3 months dosing with BIT225 in combination with IFN/RBV
- Treatment naïve, HCV gen 1 and 3
- Using new capsule formulation
- Scheduled to commence shortly

## AIMS:

- Demonstrate safety of BIT225 with 3 months dosing
- Set BIT225 up for partnering with other DAA classes



# Biotron Outlook 2013/14



# BIT225 –Multiple Market Opportunities

- **Hepatitis C**
  - Potential for future combination cocktails with polymerase and protease inhibitors
    - Unique mode of action
    - Good drug-drug interaction profile
    - Limited alternative classes for combinations (prevention of resistance)
    - Potential to fill gaps left by other DAA classes
  - Add-on to IFN/RBV treatment ex-USA
- **HIV/HCV**
  - Part of combination cocktail with either IFN/RBV and/or other new DAAs
- **HIV**
  - Add-on to anti-retroviral treatment to clean out underlying reservoirs
  - Part of future eradication or cure strategies



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